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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,805	03/26/2007	Menachem Rubinstein	30694/42147	8352

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EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

NOTIFICATION DATE	DELIVERY MODE
05/20/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/584,805	RUBINSTEIN ET AL.	
	Examiner	Art Unit	
	DONG JIANG	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's amendment filed on 03 March 2009 is acknowledged and entered. Following the amendment, claims 32-67 are canceled, and claim 31 is amended.

Currently, claim 31 is pending and under consideration.

Withdrawal of Objections and Rejections:

All objections and rejections of claims 32-36 are moot as the applicant has canceled the claims.

The lack of written description rejection of claim 31 under 35 U.S.C. 112, first paragraph is withdrawn in view of applicant's amendment.

The prior art rejection of claim 31 under 35 U.S.C. 102(b) as being anticipated by Sims et al. (US 2002/0098185 A1) is withdrawn in view of applicant's amendment.

Rejections under 35 U.S.C. §112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 31 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record set forth in the last Office Action mailed on 10/21/08, at page 3, and for the reasons below.

The newly amended claim 31 remains indefinite for the recitation of "a *therapeutically* effective IL-1 *activity inhibiting* amount", and "a *therapeutically* effective IL-18 *activity inhibiting* amount" because it is unclear what it is meant, and how or base on what such amount can be determined, i.e., is it base on the levels of IL-1 and IL-18 in a patient with a particular disease associated with IL-1 and IL-18 ("activity inhibiting"), improvement of clinical conditions of the disease ("therapeutically effctive"), or something else? Further, each different disease/condition would require different amount (to be effective) depending upon many factors.

Therefore, the recited amount cannot be determined without knowing a specific disease or condition. Furthermore, it is unclear whether "therapeutically effective" and "activity inhibiting" are the same thing. Therefore, the metes and bounds of the claim cannot be determined. Eliminating said recitation would be remedial.

Rejections Over Prior Art:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sims et al., US 2002/0098185 A1 (7/25/02, provided by applicants), and further in view of Dombroski et al. (US7,005,523), for the same reasons set forth in the prior art rejection of claims 32 and 33 under 35 U.S.C. 103(a) over the same references, on pages 6-7 of in the last Office Action mailed on 10/21/08, and for the reasons below.

The teachings of Sims and Dombroski were reviewed in the last Office Action, and are paraphrased herein:

Sims discloses the physiologically acceptable compositions of the IL-18 antagonist comprising soluble IL-18R or IL-18 binding protein in conjunction with physiologically acceptable carriers, excipients or diluents (page 5, [0046]). Further, Sims teaches methods for treating disorders characterized by elevated levels or abnormal expression of IL-18 by

administering an IL-18 antagonist such as soluble IL-18R, an IL-18 binding protein and/or an antibody (abstract, for example), wherein the disorders include rheumatoid arthritis and IBD (claim 1, for example). Furthermore, Sims teaches that the various medical disorders as being treatable with an IL-18 antagonist are treated in combination with another cytokine or cytokine inhibitor, for example, IL-18 antagonist can be administered in a composition that also contains a compound inhibiting the interaction of other inflammatory cytokines with their receptors (page 6, [0052], lines 1-7), including the use of an IL-18 antagonist in combination with an IL-1 antagonist, such as a soluble IL-1R type II molecule or an antagonist antibody to the IL-1R (page 6, [0052], the last four lines of 1st column). In addition, Sims teaches that IL-1Ra is also the IL-1R antagonist (page 13, [0147]). Sims does not explicitly mention that said combination comprises anakinra and IL-18BP, or that IL-1Ra is anakinra (Kineret as the tread name).

Dombroski teaches IL-1 inhibitors, including receptor antagonists or soluble IL-1ra (e.g. Kineret) or ICE inhibitors (column 15, lines 36-38), which can be used for the treatment of rheumatoid arthritis (column 15, lines 32-33).

Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to make a pharmaceutical composition comprising an antagonist of IL-1 such as Kineret and IL-18BP following the teachings by Sims and Dombroski. The person of ordinary skill in the art would have been motivated to do so for disease treatment such as rheumatoid arthritis as Sims and Dombroski teaches that both antagonist of IL-1 such as anakinra (Kineret) and an antagonist of IL-18 such as IL-18BP can be used for treating disorders such as rheumatoid arthritis, and reasonably would have expected success because both have been demonstrated to be able to inhibit IL-1 and IL-18, respectively.

Applicants argument filed on 03 March 2009 has been fully considered, but is not deemed persuasive for the reasons below.

At pages 5-6 of the response, the applicant argues that while a general combination of IL-18 antagonists in general with IL-1 antagonists in general is described in Sims, there is no teaching or suggestion of the specific combination of IL-18BP and anakinra; that the list of possible combinations in Sims includes not only IL-1 antagonists but also antagonists to IFNγ IL-6, IL-8, IL-12, IL-15 and TNF, particularly TNFα; that Dombroski describes numerous

possible combinations of TNFα inhibitor with other molecules, including a soluble IL-lra, e.g., Kineret, but also lists others; and that based on these extensive lists of compounds in both Sims and Dombroski, resulting in tens of thousands of possible combinations, a person of ordinary skill in the art would have required extensive experimentation to arrive to the specific claimed combination of anakinra and IL-18BP. This argument is not persuasive because it is irrelevant. As acknowledged by applicants, Sims teaches a general combination of IL-18 antagonists with IL-1 antagonists. As such, other combinations are irrelevant, and there is no need for a person of ordinary skill in the art to bother with "tens of thousands of possible combinations". All that an artisan needs to do is to use any one of the known IL-1 antagonists (for example, Kineret/anakinra, taught by Dombroski) in combination with any one of the known IL-18 antagonists (for example, IL-18BP, taught by Sims), since Sims had already taught the concept of the combination.

At page 6 of the response, the applicant argues that only when pointed out in the present application using non-permitted hindsight, a skilled artisan would have learned of the particular usefulness of the combination of anakinra and IL-18BP; that applicants unexpectedly found that IL-1 is essential for induction of IL-18BP by interferon gamma, which led to the discovery that there is a specific need to supplement IL-18BP in patients who receive medication inhibiting IL-1 to avoid the side effect of increased risk of viral infections known to be a significant side effect of Kineret monotherapy (Id., and Exhibit I). This argument is not persuasive because nowhere, in the specification or Exhibit I, it teaches that supplement IL-18BP would avoid the side effect of increased risk of viral infections. All that the specification teaches is that IL-1 is essential for induction of IL-18BP by interferon gamma, thus the inventors conceived the necessity of supplementing IL-18BP to patients with inflammatory diseases receiving medication aimed to target inhibition of IL-1 ([0041]). Further, even if it were true (supplement IL-18BP to avoid infections), it is irrelevant because the combined teachings of the prior art teach the claimed composition, and "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999).

Conclusion:

No claim is allowed.

Advisory Information:

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication should be directed to Examiner Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Dong Jiang/
Primary Examiner, Art Unit 1646
5/16/09